REMARKS

Entry of this Amendment is proper under 37 C.F.R. § 1.116 because the Amendment places the application in condition for allowance for the reasons discussed herein; does not raise any new issue requiring further search and/or consideration as the amendments amplify issues previously discussed throughout prosecution; and places the application in better form for an appeal should an appeal be necessary. Entry of the Amendment is thus respectfully requested.

As correctly indicated in the outstanding Office Action, claims 1-44 are currently pending. Claims 43-44 stand withdrawn as directed to non-elected subject matter.

Independent claims 1 and 24 have been amended herein to recite that the particles of the claimed invention are prepared from polymers which can only be dissolved in an organic solvent. Basis for these amendment may be found throughout the specification and claims as filed, especially on page 11, lines 8-14, which states that "the biodegradable polymer that can be used in the present invention is not limited to any specific material *as long as it can be dissolved in any organic solvent*" [emphasis added]. Thus, no prohibited new matter has been introduced by this Amendment.

Applicants respectfully submit that the amendments presented herein comply with 37 C.F.R. § 1.116 and thus should be entered for the following reasons. First, the amendments to claims 1 and 24 avoid the rejection set forth in the outstanding Office Action, as they further distinguish the claimed subject matter from the cited reference and support the assertion that the present claims are not obvious in light of the cited reference. Second, the amendments to the claims to not raise the issue of new matter, as addressed above. Third, the claims as amended herein do not raise any new issues requiring further search. Specifically,

when the original search was run for the claims of the present invention, the search presumably covered all possible polymers falling within the scope of the claims as filed, including those that are only soluble in an organic solvent. Thus, Applicants submit that the entry of the present amendments would not necessitate a new search.

Applicants reserve the right to pursue in a division or continuation application any subject matter canceled by way of this Amendment without prejudice or disclaimer.

REJECTIONS UNDER 35 U.S.C. § 103(a)

Claims 1-44 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Tice *et al.* in view of Ekman *et al.* Applicants note that the Office Action rejects claims 1-44 under this rejection, although claims 43-44 stand withdrawn. However, Applicants will address the rejection in terms of claims 1-44 in the interest of expediting prosecution.

Tice *et al.* is cited for purportedly disclosing a method of microencapsulating an agent by dissolving a polymer in a solvent and then adding an active ingredient. Ekman *et al.* is cited for purportedly disclosing the removal of water from a dissolved substance through the use of polyethylene glycol (PEG). The Office Action states that Ekman *et al.* only discloses the minimal removal of water, and that Ekman *et al.* discloses the benefits of the use of polyethylene glycol.

To make a *prima facie* case of obviousness, the Federal Circuit has articulated the analysis of a proper analysis under 35 U.S.C. § 103 as follows:

> [W]here claimed subject matter has been rejected as obvious in view of a combination of prior art references, a proper analysis under § 103 requires, inter alia, consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the art that they should make the

> claimed composition or device, or carry out the claimed process; and (2) whether the prior art would also have revealed that in so making or carrying out, those of ordinary skill would have a reasonable expectation of success. *See In re* Dow Chemical Co., . . . 5 U.S.P.Q.2d 1529, 1531 (Fed. Cir. 1988). Both the suggestion and the reasonable expectation of success must be founded in the prior art, not in the applicant's disclosure.

In re Vaeck, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991). It respectfully is submitted that a legally sufficient *prima facie* case of obviousness has not been adduced, because the cited art of Tice *et al.* and Ekman *et al.*, alone or in combination, do not suggest the methods claimed, let alone suggest that the claimed methods could be conducted with a reasonable expectation of success.

The present invention relates to methods of encapsulating an active substance where the polymer is initially dissolved in an organic solvent. The claims have been amended by way of the present Amendment to recite that the particles are prepared from polymers which can only be dissolved in an organic solvent.

Ekman *et al.* does not motivate the skilled artisan to use PEG as the continuous phase of the invention disclosed in Tice *et al.* Ekman *et al.* does not disclose or even suggest that microparticles could be made from polymers that are soluble in organic solvents. Rather, Ekman *et al.* focuses entirely on the preparation of microparticles made from polymers which can be dissolved in water using a two phase aqueous system. In contrast, the claims have been amended herein to recite that the polymers of the claimed invention can only be dissolved with an organic solvent.

Further, Ekman *et al.* disclose in detail methods of removing water from the inner, discontinuous, phase to form microparticles. The removal of the water is accomplished by

the addition of substances, such as PEG, to the outer phase. Thus, the skilled artisan, upon reading Ekman et al., would seek to avoid using organic solvents in favor of water-soluble polymers, and thus would be led away from the claimed invention.

Again, Applicants note that neither Ekman *et al.* nor Tice *et al.*, taken separately or in combination, would result in the claimed invention. Ekman *et al.* discloses the removal of water. The removal of water in order to solidify a polymer which was dissolved in organic solvents, as with Tice *et al.* and the present invention, would not result in the claimed invention. In fact, removing water in the attempt to solidify a polymer dissolved in an organic solvent would be unsuccessful. Thus, the cited references teach away from the present claims, as amended herein.

Finally, Applicants again note that the present invention allows the aqueous solution of PEG as a continuous phase and as an extraction medium when making microparticles from polymers that can be dissolved in organic solvents. This discovery is surprising and unexpected. The present invention also confers the new advantages of the reduction in the volume of organic solvents used, reduction in the energy of mixing used and avoidance of PVA and other surfactants.

Thus, the references, when considered alone or in combination do not render obvious the invention as claimed. Accordingly, Applicants respectfully request the appropriate withdrawal of the rejection.

CONCLUSION

In view of the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order. Such action is earnestly solicited.

In the event that there are any questions relating to this application, it would be appreciated if the Examiner would telephone the undersigned attorney concerning such questions so that prosecution of this application may be expedited.

Respectfully submitted,

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Attachment to Amendment and Reply

Marked-up Claims 1 and 24

1. (Twice Amended) A method of encapsulating an active substance in a biodegradable polymer, which comprises:

a) dissolving said biodegradable polymer in an organic solvent therefor;

b) dispersing said active substance in the organic solution obtained in step a), to provide a dispersion with the active substance as the inner phase thereof; and

c) subjecting the dispersion obtained in step (b), to an encapsulation operation with an aqueous polyethylene glycol solution as a continuous phase, such that micro- or nanoparticles having the active substance encapsulated therein are obtained;

wherein the biodegradable polymer can only be dissolved in an organic solvent.

24. (Amended) A method of encapsulating an active substance in a biodegradable polymer, which comprises:

a) dissolving said biodegradable polymer in an organic solvent therefor;

b) emulsifying said active substance, dissolved in water or other aqueous solvent therefor, in the organic solution obtained in step a), to provide an emulsion with the active substance as the inner aqueous phase thereof; and

c) subjecting the dispersion obtained in step b) to an encapsulation operation with an aqueous polyethylene glycol solution as a continuous phase, such that micro- or nanoparticles having the active substance encapsulated therein are obtained;

wherein the biodegradable polymer can only be dissolved in an organic solvent